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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
GAMETT, DANIEL C	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/891,138
Filing Date: June 25, 2001
Appellant(s): LIN ET AL.

Jean M. Lockyer, Ph.D.

For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 12/29/2005 appealing from the Office action mailed 02/20/2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is incorrect. The amendment filed under 37 C.F.R. §41.33(b)(1) on 08/11/2004, canceling claims 3, 13, 30, and 31, has been entered. Notification of entry of said amendment was mailed to Appellant on 12/12/2005.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

No evidence is relied upon by the examiner in the rejection of the claims under appeal.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

The rejection of claims 6 and 7 as failing to meet the written description requirement under 35 U.S.C. § 112, first paragraph is hereby withdrawn. Upon reconsideration, the Examiner holds that the disclosed sequences provide written description of an isolated nucleic acid encoding a polypeptide comprising an amino acid sequence of SEQ ID NO:2 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, to which claims 6 and 7 are drawn without recitation of an activity.

The following ground(s) of rejection are applicable to the appealed claims:

Claims 6 and 7 stand rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility. The detailed explanations of the scientific basis for holding that the claimed invention does not have a well-established utility and that the specification as filed does not establish a specific or substantial utility have been made of record (see Non-Final Rejection, 04/15/2003, sections 5-7) and are summarized as follows. The pending claims are drawn to an isolated nucleic acid encoding a polypeptide referred to as TGR18. The specification discloses that the amino acid sequence of TGR18 has characteristics of a G-protein coupled receptor (GPCR). There are no well-established utilities for newly discovered biological molecules. The fact that TGR18 is a

GPCR is not sufficient to infer specific utility because the superfamily of GPCRs includes over 5000 genes, which encode receptors with diverse functions, different activating ligands, different second messenger systems, and different roles in physiology. While all GPCRs share a common structural theme of having seven transmembrane domains, their amino acids sequences are highly divergent, even among subfamilies with similar functions, so it is not possible to infer activity or function from amino acid sequence alone. The specification shows that TGR18 is expressed in the kidney but does not indicate what it does there or what effect activation or inhibition of TGR18 signaling would have on kidney function. There are no working examples of a functional TGR18, and no ligand for the receptor is disclosed. All assertions of utility are nonspecific, such as can be made for any coding nucleic acid or, at best, generic to the class of G-protein coupled receptors. The asserted utilities are not substantial because the disclosure did not establish that the claimed GPCR had an activity that linked it to a physiological process or state.

Claims 6 and 7 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(10) Response to Argument

Claim Rejections - 35 USC § 101

Beginning at p.4, Appellant attempts to demonstrate that the claimed invention satisfies the requirement for utility under 35 U.S.C. § 101. The argument begins with citations of the

MPEP and case law regarding standards to address utility. The referenced sections of the MPEP point out that rejection for lack of utility should not be made if an applicant has asserted a specific, substantial, and credible utility and that a detailed explanation, including the scientific basis, must be given for any utility rejection.

Appellant's citations of *In re Langer* and *In re Gaubert* (paragraph bridging pages 4-5) are noted; however their relevance is unclear because they are directed toward cases where a specific assertion of utility has been made. The Examiner has not questioned the objective truth of any statement of utility but rather holds that the disclosure as originally filed did not assert a utility that is specific or substantial.

On p.5, first paragraph of section 2, Appellant asserts, "The invention satisfies utility under 35 U.S.C. § 101 because the identification of TGR18 nucleic acids permits one of skill in the art to analyze modulators of TGRI8." This asserted utility actually encompasses several utilities, such as use of the invention for "analysis, characterization", screening for ligands for the encoded polypeptide, and screening for compounds that regulate TGR18 expression. These asserted utilities have been addressed in the Non-Final Rejection, 04/15/2003, specifically sections 6c, 6d, and 6i, portions of which are reiterated here (asserted utilities in italics).

> c. *The isolated nucleic acid (SEQ ID NO: 1) can be used to make a polypeptide (SEQ ID NO: 2) for analysis, characterization, or therapeutic uses:* This asserted utility is not substantial nor specific. In recombinantly expressing a polypeptide, the polynucleotide is transfected into a host cell and then the protein is recovered. However, the instant specification does not disclose any known function for the claimed polypeptide or any disease state, toxin, or poison associated with SEQ ID NO: 1. In addition, this utility assertion is not specific as it can be applied to any given polynucleotide. Therefore, it is not clear how the skilled artisan would use a polypeptide manufactured by this method, for analysis, characterization, or therapeutic uses. Since significant further research would be required to determine how to use the identified polynucleotide, the asserted utility is not substantial.

d. The polypeptide (SEQ ID NO: 2) encoded by SEQ ID NO: 1 can be used to screen for a ligand: The asserted utility is also not specific, since all receptors can be used to screen for ligands.
i. The claimed nucleic acid molecules can be used in assays for drug screening to identify compounds that modulate secreted protein nucleic acid expression: This asserted utility is also not substantial. In such assays, compounds are screened for their ability to up-regulate or down-regulate expression of the nucleic acid molecule. Compounds that have on or the other activity are then labeled as potential drugs. However, the instant specification does not disclose any specific disease state wherein there is a change in SEQ ID NO: 1 expression levels or forms (i.e., mutations). Therefore, it is not clear how the skilled artisan would use a potential drug identified by this method. Since significant further research would be required to determine how to use the identified potential drugs, the asserted utility is not substantial.

In short, TGR18 nucleic acids, by themselves, do not permit one of skill in the art to analyze modulators of TGRI8. One first needs an assay of TGR18 activity. The specification provides generic descriptions of activities that GPCR are known to have, but does not indicate which one is specific to TGR18. Even if one knew how to measure TGR18 activity, screening for modulators would not be a substantial utility because, in the absence of a nexus between TGR18 and a physiological process or disease state, one would not know what to do with the modulators once they were found. Screening for substances with no utility cannot be a substantial utility.

The remainder of section 2, pages 5-6, of Appellant's Brief is a recapitulation of Examiner's prior arguments to which Appellant responds in section 3. Appellant particularly draws attention to the Examiner's prior conclusion that Lin declaration I does not establish a specific utility (final paragraph of p.5) and asserts on p. 6 (final paragraph) that Lin Declaration I demonstrates that TGR18 has a known GPCR activity, i.e., it transduces an increase in intracellular calcium. It has been pointed out (section 10, page 3 of the Final Office Action,

02/20/2004) that many GPCRs modulate changes in intracellular calcium when generally stimulated. This would be expected especially in an experimental system where a GPCR is given an opportunity to interact with promiscuous G-proteins as described in the specification at p.42, lines 26-30. Therefore, although the data presented in the Lin Declaration I show that the claimed GPCR is an active receptor, it does not reveal anything specific about the receptor.

On p.6, second paragraph of section 3, Appellant asserts: "The specification further teaches that...TGR18 can participate in the modulation of cellular function in cells, for example kidney cells, in which it is expressed (see, e.g., page 51, lines 31-34)." The cited sentence reads thusly, "For example, the activity of GPCRs (e.g., TGR18) that are expressed in a particular cell type (e.g., kidney cells), can be used to modulate cellular function (e.g., responsiveness to extracellular signals), thereby specifically modulating the function of the cells of that type in a patient." This is clearly not a "teaching" but rather it is a generic statement that includes TGR18 as a speculative example. Furthermore, it is not specific as "modulate" can indicate any kind of change; every expressed protein modulates cellular function in some way. Appellant further states "the specification also discloses that a GPCR that is predominantly expressed in the kidney can play a role in renal disease, e.g. hypertension (see, e.g., page 52, lines 2-6)". The same lines from the specification are cited again on page 8 ("Specific utility") to support the assertion that the present application discloses that TGR18 plays a role a disease condition (e.g., hypertension) that correlates with a "biological activity" i.e., GPCR activity. The cited sentence reads thusly, "For example, kidney-specific GPCRs will likely result in any of a number of nephrotic conditions or diseases..." Again, this is not a specific teaching about TGR18, but a generic

statement about GPCRs. Furthermore, the speculative phrase "will likely result in" is a far cry from a disclosure that "TGR18 plays a role".

On p.7, Appellant addresses the He *et al.* publication in which TGR18 was shown mediate an increase in intracellular calcium in response to succinic acid as ligand. Appellant further points out significant findings discussed in the He *et al.* paper, specifically that succinic acid was known to regulate re-absorption of phosphate and glucose into the proximal tubule, and to stimulate renin release. Further, He *et al.* showed that TGR18 was required for succinic acid-induced hypertension in mice. Thus, the He *et al.* paper provides some of the information that had been lacking in Lin Declaration I concerning the biological significance of succinic acid in the kidney. Had this information been included in the original disclosure, a strong argument for utility of TGR18 might have been established. However, all of these pertinent facts were learned after filing. A GPCR that transduces an increase in intracellular calcium, with succinic acid as its ligand, is not supported by the specification as filed. The terms "succinic acid" or "succinate" do not appear in the disclosure. The "teachings" of the application as filed are so general that they would have been equally valid if subsequently TGR18 had been shown to be activated by any ligand, with any of several intracellular pathways activated, in any part of the kidney, with the response being either raising or lowering of blood pressure.

At the bottom of p.8, Appellant takes issue with the Examiner's position that the asserted utility is not substantial because more research is required to determine how to use the claimed [invention]. The correctness of the Examiner's position is proven by the record. Indeed, more research was required to determine how to use the claimed invention. To wit, He *et al.*

On p. 9, Appellant argues that finding sufficient utility in the present application is consistent with the policy of encouraging early disclosure of inventions. Whether granting patent protection to the discovery of a new process or compound with a yet unknown practical utility would encourage prompt disclosure of inventions was one factor the Supreme Court carefully considered and to a significant extent relied upon in reaching its landmark decision in *Brenner v. Manson*. It is important to note that while giving due consideration to this important matter, the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion." *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966).

And,

> "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696.

The asserted utilities "valuable probes for the identification of particular cell types", "isolation of specific modulators of GPCR activity" (specification p. 6, lines 23-29); "to identify diseases, mutations, and traits caused by and associated with the GPCRs" (p. 7, lines 5-6) amount to "use testing" of the claimed invention. The application as filed does not represent a successful conclusion, but rather it is a hopeful beginning of a search.

Appellant asserts, on page 9, that the present case is analogous to *Nelson v Bowler*. To summarize, *Nelson v Bowler* was an interference proceeding. The issue was whether Nelson, the

junior party, had established utility prior to Bowler's filing date, *i.e.* also before Nelson's own filing date. The inventions at issue were prostaglandin compounds about which a great deal was previously known as they had been purified from natural sources and tested thoroughly in biological systems. The cited quote shows that the CCPA decided that tests showing pharmacological activity of the synthetic compounds were sufficient to establish patentable utility even though no specific therapeutic use for the compounds was established.

Appellant asserts that the present case is analogous to *Nelson v Bowler* because TGR18 has a physiological function in the kidney and compounds capable of modulating TGR18 are useful as agents for regulating its function. However, there are several differences in the respective fact patterns that indicate that the present case is not analogous to *Nelson v Bowler*. First, unlike prostaglandins F_2 and F_{2a}, TGR18 is not a synthetic copy of a naturally occurring substance with known physiological activities. Instead, TGR18 is a newly described member of a gene family that has over a thousand members. The present specification as filed did not disclose a physiological function for TGR18. The skilled artisan would not know how to find compounds capable of modulating TGR18, without first doing research, and then the artisan would have to do still more research to find out how modulating TGR18 activity affects kidney function. *Then* the skilled artisan would be able to decide whether TRG18 or its modulators are useful. This points to another major difference in the fact patterns of *Nelson v Bowler* and the present case, specifically, the timing involved. In *Nelson v Bowler*, the CCPA ruled that Nelson had achieved reduction to practice prior to either filing date. In the present case, it appears that reduction to practice occurred some time between the filing date and the publication of He *et al.*

Claim Rejections - 35 USC § 112--enablement

Appellant argument (p. 10, Section B) that rejection of claims 6 and 7 under 35 USC § 112, first paragraph, should be withdrawn would be persuasive only if claimed invention were supported by a specific and substantial asserted utility or a well-established utility. That is not the case, for reasons given above.

Claim Rejections - 35 USC § 112—written description

The written description rejections of claims 6 and 7 have been withdrawn. Therefore, Appellant's arguments (p. 10-12) regarding written description are moot.

For the above reasons, it is believed that the rejections of claims 6 and 7 under 35 USC § 101 and under 35 USC § 112, first paragraph should be sustained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

Respectfully submitted,

Daniel C. Gamett, Ph.D.
Art Unit 1647
28 March 2006

Conferees:

Brenda Brumback
Supervisory Patent Examiner
Art Unit 1647

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Janet Andres
Supervisory Patent Examiner
Art Unit 1649

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER